REMARKS

Claims 129-215 are pending, upon entry of the amendment submitted above. Favorable reconsideration is respectfully requested.

Applicants would like to thank Examiner Collins for the helpful and courteous discussions held with their representative on February 8 and 23, 2005. During those discussions, amendments to over come the rejections based on the applied rejections were discussed. In particular, the rejections under 35 U.S.C. §112, first paragraph, were discussed. The following remarks expand on the discussions with the Examiner.

The present invention relates to an isolated DNA sequence encoding a cdc27 protein,

where the protein comprises a NH_2-terminal domain conserved in cdc27 homologues of different origin, where the NH_2-terminal domain comprises a stretch of 161 NH_2-terminal amino acids, and wherein the stretch comprises SEQ ID NO: 6 or an amino acid sequence having at least 50% sequence identity to SEQ ID NO: 6,

where the protein contains an intact tetratricopeptide domain, and

where the protein is capable of modulating DNA replication in plant cells.

See Claim 129.

The present invention also relates to methods of using the DNA sequence to modulate plant cell and plant function. See Claims 146-175. The present invention additionally relates to plant products obtained from those methods. See Claims 176-215.

Claim 129 defines the protein of the present invention defines the *structure and the function* of the inventive protein *in detail*.

The claim specifies that the protein is a cdc27 protein and that its amino acid sequence contains SEQ ID NO: 6 or a sequence having at least 50% sequence identity to SEQ ID NO: 6 contained in a stretch of 161 NH_2-terminal amino acids. Claim 129 even explicitly requires that the NH_2-terminal domain is conserved in cdc27 homologues of different origin.

An intact tetratricopeptide domain is also specified. In terms of function, Claim 129 specifies that the protein is capable of modulating DNA replication in plant cells.

Applicants have conducted a BLAST search using SEQ ID NO: 6. A copy of the results of the BLAST search are submitted herewith. All hits obtained in the search having at least 50% sequence identity to SEQ ID NO: 6 are cdc27 proteins. Thus, even though SEQ ID NO: 6 is a relatively short sequence, it is sufficient to identify cdc27 proteins and nothing else.

The specification of the present application explicitly states that the function of the tetratricopeptide (TPR) domains is to enable the protein to interact with other proteins in the APC. The specification further states that mutation analysis in the TPR domains of yeast cdc27 revealed that intact TPRs are necessary for cdc27 function and for a functional APC. See paragraphs [0017]-[0024].

The rejections of the claims under 35 U.S.C. §112, first paragraph, as set forth at pages 4-8 of the Official Action, for an alleged lack of written description, is respectfully traversed.

As discussed above, Claim 129 defines the claimed cdc27 protein in terms of its structure and its function. In fact, the BLAST search demonstrates that SEQ ID NO: 6 or a sequence having at least 50% sequence identity thereto is sufficient to identify cdc27 proteins.

The specification provides a detailed description of the subject matter of Claim 129. The specification at paragraph [0021] states that "SEQ ID NO: 6, and thus also SEQ ID NO: 10, are part of a unique NH_2-terminal domain conserved in CDC27 homologues of different origin." SEQ ID NO: 10 is in fact the stretch of 161 NH_2-terminal amino acids specified in Claim 129. Similarly, paragraph [0017] states "The novel exon encoded by amino acid sequence SEQ ID NO: 6 [sequence omitted] is part of a unique NH_2-terminal domain

conserved in CDC27 homologues of different origin." Reference to sequences having at least 50% identity to SEQ ID NO: 6 may be found in, for example, paragraph [0009]. Thus, there is ample support in the application as filed for an NH_2-terminal domain conserved in cdc27 homologues of different origin comprising a stretch of 161 NH_2-terminal amino acids and comprising SEQ ID NO: 6 or a sequence having at least 50% identity thereto. Accordingly, Claim 129 is supported by the disclosure, and is not new matter.

In addition, there are at least three examples of sequences that fall within the scope of Claim 129 described in the present specification. Those sequences are SEQ ID NO: 6 (which encodes cdc27A1 protein), SEQ ID NO: 14 (which encodes cdc27A2 protein), and SEQ ID NO: 15 (which encodes cdc27B protein). As can be seen in the alignment presented in Figure 6 of the present application, the proteins encoded by those sequences comprise SEQ ID NO: 6 or a peptide having at least 50% amino acid identity with SEQ ID NO: 6. Thus, the specification of the present application describes multiple species within the genus embraced by Claim 129. In addition, there is an implicit disclosure of more sequences because, based on the knowledge of explicitly described cdc27 sequences, one could isolate equivalent genes from other plant species using routine experimentation. It was known at the time the present application was filed that those equivalent genes may have some sequence variation. It would be recognized that isolation of such equivalent genes from other plant species is routine once the sequence of the Arabidopsis genes are known, i.e., based on the sequences described in the present application one can readily isolate the orthologue from another plant species.

The Examiner cites the *Lilly* decision at page 7 of the Official Action. However, the facts of the present application are very different from the situation in *Lilly*.

In *Lilly*, the specification described a rat cDNA sequence and described a method of obtaining a human cDNA sequence. Significantly, the specification did not describe the

actual sequence of the human cDNA. For that reason, a claim to the human cDNA was found to lack written description in the specification.

However, in the present application, all of the features of Claim 129 are described, as discussed above. In particular, the results of the BLAST search submitted herewith demonstrates that SEQ ID NO: 6 or a sequence having at least 50% sequence identity thereto is sufficient to identify cdc27 proteins.

In view of the foregoing, the present application satisfies the written description requirement of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of these grounds of rejection is respectfully requested.

The rejection of Claims 30 and 59 under 35 U.S.C. §112, first paragraph, as set forth at pages 3-4 of the Official Action are believed to be obviated by the cancellation of those claims. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, first paragraph, for an alleged lack of enablement, is respectfully traversed. The present specification provides a detailed description of how to make and use the DNA sequence recited in Claim 129 so that the scope of the invention can be practiced without undue experimentation.

The Examiner's attention is drawn in particular to Example 4 at pages 37-39 of the specification. This Example provides ample guidance on which elements of the sequence may be modified and which elements might give rise to alteration in function/activity.

Applicants submit that as described in the present specification from page 16, line 32 to page 21, line 15, the claimed nucleic acids are isolatable from genomic libraries by routine methods. Based on the sequences of the present invention was possible to isolate a true cdc27 protein, without undue experimentation for the skilled person, because this isolation can be done by routing experiments like hybridization or PCR.

The Examiner states that cdc27 proteins have 16 different exons. The Examiner raised the concern that the effect of a peptide having only 1 exon (SEQ ID NO 6) is unpredictable. To meet the Examiner's concern, Claim 129 specifies that the protein comprises SEQ ID NO: 6 and is capable of modulating DNA replication in plant cells. That recitation is supported by the specification at page 6, lines 23-25, which states that the presence of exon SEQ ID NO: 6 is responsible for promoting APC-substrate action and DNA replication. It is further supported by the common knowledge that the N-terminus of cdc27 proteins harbors the highly conserved in CDC27/NUC2-LIKE domain (see description at page 7 of WO 01/02430, lines 36-37). SEQ ID NO 6: (VNLQLLARCYLSNSQAYSAYY ILKGSK) is a large portion of this conserved domain. Therefore, it is submitted that the effect of the presence of SEQ ID NO: 6 is a functional effect of the protein, which functional effect is to the promote APC substrate action and therewith DNA-replication.

With respect to "undue experimentation," the specification of the present application provides guidance to use proteins comprising SEQ ID NO 6, which is part of a stretch of at least 161 amino acids, which is part of a cdc27 domain and which is part of a protein with the biological function of modulating DNA replication. No undue experimentation is necessary since the presence of SEQ ID NO: 6 is related to the biological function of the protein as it contributes to APC substrate activity and therewith in DNA replication.

The other Examples of the present application also provide explicit teaching for making and using the claimed DNA sequence.

Example 2 describes the isolation of the cdc27A1 gene, which is an example of a sequence which comprises SEQ ID NO: 6 and is capable of modulating DNA replication in plant cells.

Example 5 relates cdc7, and is relevant for the description of the cloning steps and vectors, which are referred to in the Examples which relate to SEQ ID NO: 6.

Example 6 is a prophetic example of how to obtain male sterility in plants using a cdc27 protein which is mutant and which is cloned under control of a tapetum specific example and therefore disrupts cell division.

Example 7 is a hypothetical example which describes that the cdc27 muteins can be used to increase endoreduplication as mentioned in Example 4. Example 7 provides additional details on how to clone the mutants and to transform them into plants.

Example 8 describes a study of the natural expression occurrence of the cdc27 protein, which comprises SEQ ID NO: 6.

Example 9 describes cloning a gene encoding a cdc27B protein, which comprises SEQ ID NO: 6.

Example 10 describes the cloning of cdc27B protein, which comprises a peptide that is at least 50% identical to SEQ ID NO: 6.

In addition, Applicants have also conducted the experiments described below.

Transformation of Tobacco with cdc27A1

Tobacco plants were transformed with a 35S::Atcdc27A1 construct. These plants showed improved characteristics (or improved or useful phenotypes) such as improved growth characteristics, which is manifested by improved yield, improved plant height and improved biomass. See Figure 2 submitted with the response filed on July 20, 2004. In addition, more cell division, which is manifested by more branching was also observed (see Figure 2). The plants transformed plants also had more leaves as shown in Figure 3 attached hereto and bigger leaves as shown in Figure 4 submitted with the response filed on July 20, 2004.

Transformation of Arabidopsis with cdc27B

Arabidopsis plants were transformed with a 35S::Atcdc27B construct and the resulting plants showed improved characteristics (or improved or useful phenotypes) such as improved growth characteristics manifested by stay-green phenotype. See Figure 5 submitted with the response filed on July 20, 2004. Figure 5 also shows that the transformed cells had more cell division as manifested by more branching and more leaves.

In view of the foregoing, the claims of the present application satisfy the criteria for enablement. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejections of Claims 86 and 89-93 under 35 U.S.C. §101 and §102(b) are believed to be obviated by the amendments submitted above. The newly-added claims have been drafted in incorporate the Examiner's suggestions with respect to Claims 89, 90 and 92. Accordingly, withdrawal of those grounds of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, second paragraph, is believed to be obviated by the amendments submitted above. In the newly-added claims, the language identified by the Examiner has either been modified or the subject matter of the claim is not recited therein (Claims 80 and 125).

The objection to the claims (see page 3 of the Official Action dated October 6, 2004) is believed to be obviated by the amendment submitted above in part and is in part respectfully traversed.

The objection to Claims 30, 32-33, 59 and 61-62 has been addressed in the newly-added Claims.

Regarding Claims 41-45 and 70-74, which correspond to newly-added Claims 141-142 and 164-165, just because one sequence has been elected does not forbid a dependent claim from specifying another sequence. Specifically, the elected sequence defines an amino acid sequence. SEQ ID NO: 9 is a DNA sequence which encodes that amino acid sequence.

There is nothing improper about this. In fact, the dependent claims are allowable for the same reasons as the independent claim. Accordingly, the rejoinder provisions of MPEP §821.04 apply to the subject matter of Claims 41-45 and 70-74. Accordingly, withdrawal of the objections is respectfully requested.

Regarding the Restriction Requirement, Claim 48 corresponds to newly-added Claim 145. Claim 143 ultimately depends from Claim 129. Since Claim 129 is allowable as discussed above, it is irrelevant that that Claim 145 contains additional subject matter. The dependent claim is patentable for the same reasons as the independent claim from which it depends. Similarly, Claim 171 ultimately depends from Claim 129, which is allowable as discussed above. Therefore, the rejoinder provisions of MPEP §821.04 apply to Claims 145 and 171. Accordingly, those claims should be rejoined with the elected subject matter. Such rejoinder is requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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NCBI **results of BLAST**

TBLASTN 2.2.10 [Oct-19-2004]

Reference:
Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

RID: 1109155120-16916-67107064156.BLASTQ2

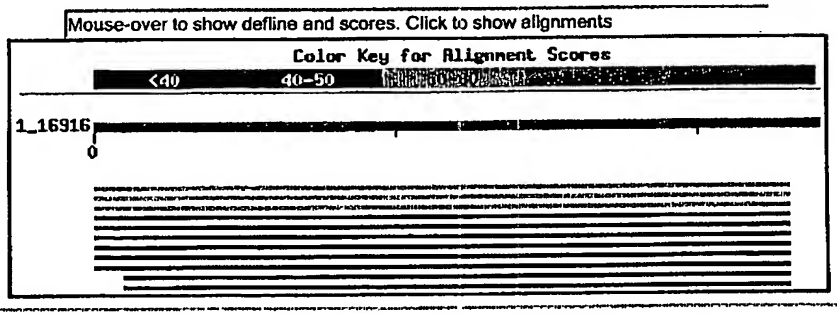
Query=
(24 letters)

Database: All GenBank+EMBL+DDBJ+PDB sequences (but no EST, STS, GSS, environmental samples or phase 0, 1 or 2 HTGS sequences)
2,902,356 sequences; 13,331,710,082 total letters

If you have any problems or questions with the results of this search please refer to the BLAST FAQs

Taxonomy reports

Distribution of 11 Blast Hits on the Query Sequence



Sequences producing significant alignments:	Score (bits)	E Value	
gi|4220645|dbj|AB023046.1| Arabidopsis thaliana genomic DNA...	51	2e-05	
gi|18401090|ref|NM_112503.1| Arabidopsis thaliana cell divi...	51	2e-05	G E
gi|2062153|gb|AC001645.1|ATAC001645 Arabidopsis thaliana ch...	51	2e-05	E
gi|21304446|emb|AJ487669.1|ATH487669 Arabidopsis thaliana m...	40	0.045	G
gi|42469423|emb|BX819164.1|CNS0AA15 Arabidopsis thaliana Fu...	40	0.045	
gi|22136203|gb|AY128780.1| Arabidopsis thaliana CDC27/NUC2-...	40	0.045	
gi|20197566|gb|AC006081.4| Arabidopsis thaliana chromosome ...	40	0.045	E
gi|17064787|gb|AY062470.1| Arabidopsis thaliana CDC27/NUC2-...	40	0.045	
gi|30680845|ref|NM_179663.1| Arabidopsis thaliana cell divi...	40	0.045	G E
gi|58531193|dbj|AP008212.1| Oryza sativa (japonica cultivar...	38	0.13	
gi|51090822|dbj|AP003539.3| Oryza sativa (japonica cultivar...	38	0.13	

Alignments

Get selected sequences | Select all | Deselect all

>gi|4220645|dbj|AB023046.1| Arabidopsis thaliana genomic DNA, chromosome 3, P1 clone: MYA6
Length = 75289

Score = 51.2 bits (121), Expect = 2e-05
Identities = 24/24 (100%), Positives = 24/24 (100%)
Frame = +3

```
Query: 1     VNLQLLARCYLSNSQAYSAYYILK 24
              VNLQLLARCYLSNSQAYSAYYILK
Sbjct: 42990 VNLQLLARCYLSNSQAYSAYYILK 43061
```

>gi|18401090|ref|NM_112503.1| Arabidopsis thaliana cell division cycle family protein / CDC family protein (At3g16320) mRNA, complete cds
Length = 2184

Score = 51.2 bits (121), Expect = 2e-05
Identities = 24/24 (100%), Positives = 24/24 (100%)
Frame = +1

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Query: 1   VNLQLLARCYLSNSQAYSAYYILK 24
            VNLQLLARCYLSNSQAYSAYYILK
Sbjct: 106 VNLQLLARCYLSNSQAYSAYYILK 177
```

>gi|2062153|gb|AC001645.1|ATAC001645 Arabidopsis thaliana chromosome III BAC T02004 genomic sequence, complete sequence
Length = 91714

Score = 51.2 bits (121), Expect = 2e-05
Identities = 24/24 (100%), Positives = 24/24 (100%)
Frame = -3

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Query: 1     VNLQLLARCYLSNSQAYSAYYILK 24
              VNLQLLARCYLSNSQAYSAYYILK
Sbjct: 74687 VNLQLLARCYLSNSQAYSAYYILK 74616
```

>gi|21304446|emb|AJ487669.1|ATH487669 Arabidopsis thaliana mRNA for HOBBIT protein (hbt gene)
Length = 2877

Score = 39.7 bits (91), Expect = 0.045
Identities = 18/24 (75%), Positives = 21/24 (87%)
Frame = +2

```
Query: 1   VNLQLLARCYLSNSQAYSAYYILK 24
            VNLQLLA  YL N+QAYSAY++LK
Sbjct: 506 VNLQLLATSYLQNNQAYSAYHLLK 577
```

>gi|42469423|emb|BX819164.1|CNS0AA15 Arabidopsis thaliana Full-length cDNA Complete sequence from clone GSLTFB53ZC03 of Flowers and buds of strain col-0 of Arabidopsis thaliana (thale cress)
Length = 2508

Score = 39.7 bits (91), Expect = 0.045
Identities = 18/24 (75%), Positives = 21/24 (87%)
Frame = +3

```
Query: 1   VNLQLLARCYLSNSQAYSAYYILK 24
            VNLQLLA  YL N+QAYSAY++LK
Sbjct: 180 VNLQLLATSYLQNNQAYSAYHLLK 251
```

>gi|22136203|gb|AY128780.1| Arabidopsis thaliana CDC27/NUC2-like protein (At2g20000) mRNA, complete cds
Length = 1915

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 Score = 39.7 bits (91), Expect = 0.045
 Identities = 18/24 (75%), Positives = 21/24 (87%)
 Frame = +1

Query: 1   VNLQLLARCYLSNSQAYSAYYILK 24
           VNLQLLA  YL N+QAYSAY++LK
Sbjct: 106 VNLQLLATSYLQNNQAYSAYHLLK 177
```

>gi|20197566|gb|AC006081.4| Arabidopsis thaliana chromosome 2 clone T2G17 map mi148, complete sequence

```
          Length = 97814

 Score = 39.7 bits (91), Expect = 0.045
 Identities = 18/24 (75%), Positives = 21/24 (87%)
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           VNLQLLA  YL N+QAYSAY++LK
Sbjct: 82586 VNLQLLATSYLQNNQAYSAYHLLK 82657
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>gi|17064787|gb|AY062470.1| Arabidopsis thaliana CDC27/NUC2-like protein (At2g20000; T2G17.20) mRNA, complete cds

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          Length = 2672

 Score = 39.7 bits (91), Expect = 0.045
 Identities = 18/24 (75%), Positives = 21/24 (87%)
 Frame = +3

Query: 1   VNLQLLARCYLSNSQAYSAYYILK 24
           VNLQLLA  YL N+QAYSAY++LK
Sbjct: 174 VNLQLLATSYLQNNQAYSAYHLLK 245
```

>gi|30680845|ref|NM_179663.1| Arabidopsis thaliana cell division cycle family protein / CDC family protein (At2g20000) mRNA, complete cds

```
          Length = 2878

 Score = 39.7 bits (91), Expect = 0.045
 Identities = 18/24 (75%), Positives = 21/24 (87%)
 Frame = +2

Query: 1   VNLQLLARCYLSNSQAYSAYYILK 24
           VNLQLLA  YL N+QAYSAY++LK
Sbjct: 506 VNLQLLATSYLQNNQAYSAYHLLK 577
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>gi|58531193|dbj|AP008212.1| Oryza sativa (japonica cultivar-group) genomic DNA, chromosome 6, complete sequence

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 Score = 38.1 bits (87), Expect = 0.13
 Identities = 16/23 (69%), Positives = 20/23 (86%)
 Frame = -3

Query: 2         NLQLLARCYLSNSQAYSAYYILK 24
           N+QLLA CYL N+Q Y+AY+ILK
Sbjct: 24649732 NVQLLATCYLHNNQPYAAYHILK 24649664
```

>gi|51090822|dbj|AP003539.3| Oryza sativa (japonica cultivar-group) genomic DNA, chromosome 6, PAC clone:P0040H10

```
          Length = 173301

 Score = 38.1 bits (87), Expect = 0.13
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```
 Identities = 16/23 (69%), Positives = 20/23 (86%)
 Frame = -3

Query: 2       NLQLLARCYLSNSQAYSAYYILK 24
                N+QLLA CYL N+Q Y+AY+ILK
Sbjct: 132925 NVQLLATCYLHNNQPYAAYHILK 132857
```

Get selected sequences | Select all | Deselect all

```
Lambda     K      H
   0.325    0.133    0.378

Gapped
Lambda     K      H
   0.267   0.0410    0.140

Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
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Number of Hits to DB: 70,295,811
Number of extensions: 237682
Number of successful extensions: 1541
Number of sequences better than 10.0: 4
Number of HSP's better than 10.0 without gapping: 1511
Number of HSP's gapped: 1541
Number of HSP's successfully gapped: 4
Number of extra gapped extensions for HSPs above 10.0: 0
Length of query: 24
Length of database: 13,331,710,082
Length adjustment: 0
Effective length of query: 24
Effective length of database: 4,443,903,360
Effective search space: 106653680640
Effective search space used: 106653680640
T: 13
A: 40
X1: 15 ( 7.0 bits)
X2: 38 (15.0 bits)
X3: 64 (25.0 bits)
S1: 40 (22.0 bits)
S2: 75 (33.5 bits)
```